UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/332,866	06/15/1999	BEATRICE LEVEUGLE	A52026US	3446

32254 7590 12/03/2002

KEOWN & ASSOCIATES
500 WEST CUMMINGS PARK
SUITE 1200
WOBURN, MA 01801

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/03/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/332,866	LEVEUGLE ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,15,17,20,21 and 28-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-15, 17, 20-21, 28-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 14-15, 17, 20,-21, 28-34 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Rejection under 35 USC 112, first paragraph of claims 14-15, 17, 20,-21, 28-34, pertaining to a method for inducing an immune response to prostate specific antigen in a patient, or a method for inducing a host to produce an antibody that specifically binds to prostate specific antigen, remains for reasons already of record in paper No.19.

Applicant argues that Example 11, in which pre-administration of mAb AR47.47 allows sufficient time for an effective immune response to develop, more closely mimics the human prostate cancer situation. In Example 11, there is a clear difference between mAb AR47.47 treated mice and control mice, and thus one would predict that the treatment of prostate cancer in human would be effective.

Applicant further argues that new claims 28-34 do not recite a therapeutic benefit, and are therefore fully supported by Examples 5-8. Such experiments are useful

for determining the effects of varying levels of circulating PSA on e.g. precancerous patients.

Applicant asserts that despite some false positive control, the positive results for Ab2 were obtained in experiments 10 and 14 (p.38, line 10), and both Ab2 and Ab3 were obtained in experiments 10 and 14 (p.39, on top of page).

Applicant asserts that the rejection is based on T-cell anergy and should be limited to claims 14, 15, 17 and 20-21. Applicant asserts that Sherman et al teach that it may be possible to activate the residual T-cell repertoire to the extent necessary to prevent tumor cell growth, and that because it is generally the case that tumor associated antigens are expressed at a higher level than normal tissue, these results encourage the prospect of eliminating tumor without induction of autoimmunity. Applicant concludes that Sherman et al actually supports the likelihood of success of the claimed invention.

Applicant further asserts that the specification discloses how to avert such T-cell anergy, such as presentation of cryptic epitopes to which anergy has not been established and that this mechanism is supported by a recent publication by Berlyn et al, in which a combination of PSA, dendritic cells and mAb 47.47 leads to an immune response against two unrelated PSA peptides.

The recitation of Berlyn et al is acknowledged.

Applicant's arguments set forth in paper No.23 have been considered but are not deemed to be persuasive for the following reasons:

Contrary to Applicant assertion, Example 11 is not representing the human prostate cancer situation. In Example 11, mice are cancer-free while being treated with the claimed antibody, before injection of a tumor cell line. Further, the claims do not recite the limitation of pretreatment of a subject with the claimed antibody, before said subject develops prostate cancer.

Further, from experiments 8, 13 and 10, 14 in Balb/c mice and DBA mice, respectively, with tumor burden, it is not clear whether Ab2 and especially Ab3 are produced. Although Ab2 are obtained in experiments 10 and 14 (p.38, line 10), Ab2 is not found in experiment 13 and the amount of Ab2 seems to be non-significant (+ and -) in experiment 8 (p.37). Moreover, for Ab3, in three out of four experiments, i.e. experiments 8, 10, 14, the negative controls have positive results for Ab3, and no difference between the controls and Ab3 is found in all four experiments (p.37-38). Further, although both Ab2 and Ab3 are obtained in experiment 10 (p.39, on top of page), both Ab2 and Ab3 are not obtained in experiment 14 (p.39, on top of page). Similarly, although both Ab2 and Ab3 are obtained in experiment 8, both Ab2 and Ab3 are not obtained in experiment 13 (p.38, on top of page).

In addition, as stated in the previous Office action, it is unpredictable that Ab3 is actually detected in the present invention. The specification discloses that the presence of Ab3 is only detected when in an assay for detecting Ab3, the plate is coated with PSA (p.31), and thus it is possible that the Ab3 detected by Applicant is an antibody that is not Ab3, wherein said antibody binds to an epitope on PSA which is different from the claimed epitope of SEQ ID NO:1.

Moreover, even if the presence of Ab2 in the claimed invention is significant, the claims are drawn to a method for inducing an immune response to prostate specific antigen in a patient, or a method for inducing a host to produce an antibody that specifically binds to prostate specific antigen, and not a method for inducing the production of Ab2. As disclosed in the specification on page 6, the Ab2 could bind to either the antigen binding site of Ab1, i.e. mimics the structure of the antigen epitope, or an idiotope of Ab1 that is distinct from the antigen binding site. Thus the presence of Ab2, which does not bind to prostate specific antigen, does not correlate with the claimed methods for inducing an immune response to prostate specific antigen in a patient, or for inducing a host to produce an antibody that specifically binds to prostate specific antigen.

Concerning examples 5-8, Example 5 discloses production of Ab2 in mice without tumor burden; Example 6 discloses detection of Ab3 in a host, which seem to be mice without tumor burden; Example 7 discloses tumor development in mice that are treated with anti-PSA antibody RLSD09, which is not the claimed antibody. Further, the mice are pretreated with said antibody RLSD09, before injection of a tumor cell line, i.e. the mice are tumor free when first treated with the antibody. Example 8 discloses detection of Ab3 from the injection of the claimed antibody Ar 47.47 in mice that do not seem to have tumor burden. Thus Examples 5-8 disclose production of antibodies from mice that seem not to have a tumor burden, and do not support the claims 14, 15, 17 and 20-21, nor the claims 28-34, which encompass a method for inducing an immune response to prostate specific antigen in a patient with prostate cancer, or a method for

inducing a host with a tumor burden to produce an antibody that specifically binds to prostate specific antigen.

Moreover, the problem with T-cell anergy would apply as well to claims 28-34, besides to claims 14, 15, 17, 20-21, because one would not have expected any significant amount of antibody specific for the tumor would be produced in a host with tumor burden. It is well known in the art that T-cell anergy blocks the cytotoxic and proliferative response of tumor-specific T cells (Sherman et al, Smith et al, all of record), and thus it is unpredictable that proliferative T cells that are needed for B cells activation and producing antibodies would not be anergic in patients with tumor burden.

In addition, Sherman et al do not support the claimed invention. Although Sherman et al teach that it may be possible to activate the residual T-cell repertoire to the extent necessary to prevent tumor cell growth, it is unpredictable that the activation of residual T-cell repertoire is adequate for treating tumors. Actually Example 12 of the specification confirms this statement, which discloses that no therapeutic effect is seen in mice with tumor burden which are treated with the claimed antibody AR 47.47.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Rejection under 35 USC 112, first paragraph of claims 14-15, 17, 20,-21, pertaining to a method for inducing an immune response to prostate specific antigen in a patient, comprising administering "any binding agent" that specifically binds to an epitope, wherein said epitope is specifically bound by the antibody produced by the hybridoma HB-12526, remains for reasons already of record in paper No.19.

Applicant argues that the nature of the target sequence and not the binding agent should be important. Applicant asserts that the present invention has surprisingly discovered a target which, when bound, leads to presentation of the binding agent-PSA complex in a manner leading to a multi-epitopic response.

Applicant's arguments set forth in paper No.23 have been considered but are not deemed to be persuasive for the following reasons:

The claimed invention encompasses a method for production of an immune response to prostate specific antigen, or a method for producing anti-idiotypic antibodies which in turn produce anti-anti-idiotypic antibodies which recognize an epitope of antibody mAb 47.47, comprising administering any binding agent having any structure, that binds to the epitope of antibody mAb 47.47. One cannot predict that administration of a binding agent, .e.g. a label, that binds to the epitope of antibody mAb 47.47 would produce an immune response to prostate specific antigen, because the structure of said binding agent is totally unrelated to prostate specific antigen. Further, one cannot predict that any binding agent with any structure unrelated to the claimed antibody mAb 47.47, e.g. a label, would produce anti-idiotypic and anti-anti-idiotypic antibodies, because based on the teaching of Stites et al, of record, anti-idiotypic antibodies are produced from the first antibody and not from any binding agent having any structure unrelated to that of the claimed antibody mAb 47.47.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

November 21, 2002

SUSAN UNGAR, PH.D
PRIMARY EXAMINER